REMARKS

Status Summary

Claims 1-20 were pending in the present application. Applicants elected Group I, Claims 1-10 in response to a Restriction Requirement. Claims 11-20 have been withdrawn from further examination by the U.S. Patent and Trademark Office, hereinafter "the Patent Office", as being drawn to a non-elected groups. Claims 11-20 have been canceled by the present amendment without prejudice. Applicants hereby reserve the right to file one or more divisional patent applications directed to the unelected subject matter.

Claims 1-10 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Further, Claims 2 and 10 have been objected to for certain informalities. Finally, Claims 1, and 3-9 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Published U.S. Patent Application No. 2003/0068825.

In the present amendment, Applicants have amended Claims 1, 2, and 10 to more particularly recite the subject matter claimed therein. No new matter has been added.

Sequence Listing

The Patent Office asserts the Sequence Listing filed June 28, 2002 does not comply with the requirements of 37 C.F.R. § 1.821 – 1.825 because the Sequence Listing was not accompanied by a Statement that the content of the paper and computer readable copies include no new matter.

The Sequence Listing filed June 28, 2002, includes only sequences previously disclosed in the pending application as filed and therefore assert that the paper and computer readable copies of the Sequence Listing do not introduce new matter. A statement to this effect is attached. Accordingly, applicants respectfully request withdrawal of the objection to the Sequence Listing.

Specification

The Patent Office has indicated that the substitute specification filed June 28, 2002 is approved. However, the Patent Office has objected to the Abstract of the Disclosure because it allegedly is "insufficiently detailed as to the basic structure of the compounds which form part of the elected invention." Official Action at page 2, section 3. Applicants have amended the Abstract to include Formulas II and III, as recited in the pending claims. No new matter has been added. Applicants therefore respectfully request withdrawal of the objection to the Abstract.

The Patent Office has also objected to paragraph [0019] on page 15 of the specification because the Patent Office asserts a SEQ ID NO. needs to be inserted into the paragraph. This change to the specification has been made as indicated by the amendment to the specification above. No new matter has been added. Applicants therefore respectfully request withdrawal of this objection to the specification.

Claim Rejection - 35 U.S.C. § 112

Claims 1-10 stand rejected by the Patent Office under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

The Patent Office has rejected Claims 1-10 under 35 U.S.C. § 112, second paragraph as indefinite because the Patent Office alleges the structures of the compounds being claimed is unclear. The Patent Office argues with respect to Formulas II and III and the –NH-X- groups, that when X is an amino acid sequence, it is unclear if the sequence is oriented in the conventional direction (5'-3'), or with the C-terminus at the left-hand side. The Patent Office asserts groups Y and Z are also indefinite for similar reasons.

In response, Applicants wish to clarify that when X is an amino acid sequence, as recited in Formulas II and III, the "NH" before the "X" is presented to clearly show that the "Acyl" group is attached to the terminal NH of the amino acid chain, and not, for example, to an R group side chain, or that the amino acid sequence is reversed from conventional nomenclature. Specific compounds disclosed in the present application supporting this can be found in the specification at paragraphs [0067] – [0068], wherein compounds of SEQ ID NOs.: 2-16 and 41-44 are disclosed. Therefore, Applicants respectfully submit the –NH-X- groups of Formulas II and III, when X is an amino acid sequence, is not indefinite in that the nomenclature indicates the terminal NH of the amino acid chain directly connects to the Acyl group, rather than by a side chain.

Likewise, with groups Y and Z, as recited in Formulas II and III, the presence of "-C(O)-NR- of group Y indicates the connection of the carboxyl group of the 3' amino acid in the Epitope Tag Site with the 5' amino group of the Protease Cleavage Site in the conventional 5' to 3' orientation of amino acid sequences, with or without additional amino acids as defined in group Y. Again, specific compounds found throughout the specification and in particular at paragraphs [0067] – [0068] illustrate the traditional orientation of amino acid sequences linked within the compounds. With group Z, the amide bonds shown are intended to indicate that any amino acid sequences linked to Z, or forming part of Z are done so either in the standard nomenclature 5' to 3' binding of the terminal NH to the terminal CO, or in the reverse direction. Therefore, Applicants respectfully submit Claims 1-10 are not indefinite, as asserted by the Patent Office, and request withdrawal of the rejection based on 35 U.S.C. § 112, second paragraph.

The Patent Office has also rejected Claim 1 under 35 U.S.C. § 112, second paragraph, as being indefinite due to the recitation that Link can be Arg-δ-iodoacetamide. The Patent Office argues such a structure would be sterically hindered if the iodoacetamide is linked to the δ atom. Applicants have deleted the Arg-δ-iodoacetamide species from the Link Markush group, thereby obviating the rejection. As such, Applicants respectfully request withdrawal of the rejection of Claim 1 under 35 U.S.C. § 112, second paragraph.

The Patent Office has also rejected Claims 1 and 2 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Patent Office asserts that it is not

possible to correspond the generic formulas recited in Claim 1 with the specific examples recited in Claims 2 and 10. Specifically, the Patent Office asserts that the examples recited in Claim 2 should be interpreted to mean that the ornithine or lysine residues at the ends of the compounds are intended to include groups in addition to the side chains of these compounds, rather than modification of the side chains, with iodoacetamide because the last compound recited in Claim 2 requires a C-terminal ornithine residue (which has a three-carbon atom side chain) along with the presence of a four-carbon atom group.

Applicants respectfully traverse the Patent Office's interpretation of the compounds recited in Claim 2 and submit that the specific examples of Claim 2 are in fact encompassed by the generic formulas recited in Claim 1.

First, Applicants note that the last compound recited in Claim 2 contained a typographical error, which has been corrected by the present amendment to the claims. Specifically, the last compound recited in Claim 2 contained one additional "CH_2", which has been deleted by amendment to Claim 2. Support for this amendment can be found at paragraphs [0064] - [0066] of the subject U.S. patent application as filed. No new matter has been added.

When Claim 2 is read as amended to correct the typographical error, and in light of Claim 1 from which it depends, it is clear that the group at the end of the claimed compounds (affixed to the lysine or ornithine) is the lysine or ornithine side-chain, derivatized by an iodoacetamide group. This reading of the compounds of Claim 2 agrees with Claim 1, from which it depends, in that Link is selected from the

group consisting of Lys-ϵ-iodoacetamide, and Orn-δ-iodoacetamide. Also, the specification teaches at page 26, paragraphs [0064] – [0066] that when an amino acid group of a compound is derivatized by an iodoacetamide group, the iodoacetamide group is chemically bound to the side-chain amino group of the amino acid moiety. Further, the present specification at paragraph [0065] specifically illustrates the formula for Lys-ϵ-iodoacetamide, which it indicates has the formula $ICH_2C(O)NH(CH_2)_4CH(NH_2)COOH$. Therefore, with the amendment to correct the typographical error of Claim 2, it is evident that the specific compounds recited in Claim 2 correspond with the generic formulas recited in Claim 1, from which Claim 2 depends. It is further evident that the specific compounds recited in Claim 2 should read to indicate that the iodoacetamide is derivatized off the side-chain of the terminal amino acid of the compound. As such, Applicants respectfully submit Claims 1 and 2 are not indefinite and request withdrawal of the rejection of Claims 1 and 2 under 35 U.S.C. § 112, second paragraph.

In light of the above remarks with regard to the rejections of Claims 1-10 under 35 U.S.C. § 112, second paragraph, Applicants respectfully submit the rejections have been obviated, and request withdrawal of the rejections of Claims 1-10 as indefinite. Applicants also respectfully submit the claims are now in proper condition for allowance and earnestly request a Notice of Allowance to that effect.

Claim Objection

The Patent Office has objected to Claim 10 because of certain informalities. Specifically, the Patent Office asserts that the abbreviation "A" used as the commonly known one letter abbreviation for "alanine" must be changed because this abbreviation is already used in Claim 1, formula II. Applicants have amended Claim 10 to place it in independent form. Applicants respectfully submit the amendment to Claim 10 obviates the objection, as Claim 10 no longer depends from Claim 1. Therefore, Applicants respectfully request withdrawal of the objection to Claim 10 and further request allowance of Claim 10.

The Patent Office has objected to Claims 2 and 10 under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. First, the Patent Office asserts that Claim 2 recites compounds that do not appear to comprise a Lys-ϵ-iodoacetamide, an Arg-δ-iodoacetamide, or an Orn-δ-iodoacetamide group, as required by independent Claim 1. Applicants have amended Claim 2 to correct the typographical error as discussed above, and further have indicated the compounds of Claim 2 are supported by the generic formulas of Claim 1 in that the side-chain group of the terminal amino acid of the listed compounds is derivatized by iodoacetamide, as discussed in detail above. The Patent Office also asserts that the compounds of Claim 10 do not appear to comprise an –NH- group adjacent to the Acyl group as required by formula III of Claim 1. Applicants have amended Claim 10 to independent form, which Applicants respectfully submit obviates this objection. Finally, the Patent Office objects to Claim

10, asserting the compounds of Claim 10 do not comprise a Lys-ϵ-iodoacetamide, an Arg-δ-iodoacetamide, or an Orn-δ-iodoacetamide group as required by independent Claim 1. Again, Applicants have amended Claim 10 to independent form, which Applicants respectfully submit obviates this objection.

In light of the above remarks, Applicants respectfully request withdrawal of the objection to Claims 2 and 10 and further request allowance of Claims 2 and 10.

Claim Interpretation

The Patent Office has interpreted the compounds of Claim 2 as requiring an amino group adjacent to the Acyl group in addition to the amino group which is present in the N-terminal cysteine residue. Applicants respectfully submit this interpretation is incorrect. As discussed above, the -NH- indicates that the Acyl group is attached directly to the amino group at the 5' end of the first amino acid residue, rather than bonded to a side-chain of the amino acid, and further indicates that the amino acid chain is written in conventional nomenclature, that is, in the 5' to 3' direction. Applicants respectfully submit this interpretation is consistent with the formulas of independent Claim 1, from which Claim 2 depends, as well as the teachings of the specification.

Claim Rejection – 35 U.S.C. § 102(e)

Claims 1 and 3-9 have been rejected by the Patent Office under 35 U.S.C. § 102(e) as being anticipated by Published U.S. Patent Application No. 2003/0068825 to Washburn et al. (hereinafter referred to as "Washburn et al."), claiming priority to U.S. Provisional Patent Application No. 60/305,169. The Patent Office argues

Washburn et al. teaches compounds having the same structures recited in Claims 1 and 3-9.

The position of the Examiner as summarized above with respect to Claims 1, and 3-9 is respectfully traversed as described below.

"A claim is anticipated only if each and every element in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Claim 1 presently recites a compound of Formula II or III:

(II) Acyl-NH-X-[Epitope Tag Site]$_A$-Y-[Protease Cleavage Site]-Z-Link

(III) Acyl-NH-X-alk-O-Ph-CH_2-Z-Link

where:

A is an integer from 0 to 12;

X is selected from the group consisting of an amide bond of formula -C(O)-NR-, a carbonyl of formula -C(O)-, and an amino acid sequence comprising 0 to 3 amino acids, where R is hydrogen or lower alkyl;

Y is an amide bond of formula -C(O)-NR-, where R is hydrogen or lower alkyl, or Y is an amino acid sequence comprising between 0 to 10 amino acids;

Z is selected from the group consisting of an amide bond of formula -$(CH_2)_B$-C(O)-NR-, an amide bond of formula -$(CH_2)_B$-NR-C(O)-, and an amino acid sequence comprising between 0 to 3 amino acids,

where R is hydrogen or lower alkyl, and

where B is an integer from 0 to 20;

alk is straight or branched chain of alkylene comprising between 0 and 5 carbon atoms;

Ph is a phenyl group optionally substituted with one or more methoxy or nitro groups ortho or para to the -CH_2-group;

Link is selected from the group consisting of Lys-ϵ-iodoacetamide and Orn-δ-iodoacetamide;

Epitope Tag Site is a sequence of amino acids,

where when A is two or more, the amino acid sequence of each Epitope Tag Site can be the same or different; and

Protease Cleavage Site is an amino acid sequence of SEQ ID NO: 1 that is a cleavage site for TEV protease.

Claim 1 has been amended to more particularly recite that X of Formulas II and III can be an amino acid sequence comprising 0 to 3 amino acids. Support for the amended amino acid numerical range can be found throughout the specification by the teaching of specific exemplary compounds. For example, X is 1 amino acid (alanine) in the compounds of SEQ. ID. NOs.: 2-35, wherein the Epitope Tag Site comprises the amino acid sequence set forth in SEQ. ID. NO.: 38 (YPYDVPDYA), and identified as an Epitope Tag Site in the specification at paragraphs [0114]-[0116]. Further, specific examples wherein X is 3 amino acids (CAS) are specifically recited in the compounds of SEQ. ID. NO.: 41-44, wherein X is CAS, the Epitope Tag Site and Y are absent, and the Protease Cleavage Site is SEQ. ID. NO.: 1 (ENLYFQG),

as noted in paragraph [0055] and recited in Claim 1. Therefore, Applicants respectfully submit the amendment of the range of amino acids recited in the definition of element "X" in Claim 1 to 0 to 3 is specifically supported by exemplary compounds recited in the specification. Therefore, no new matter has been added by the amendment.

Washburn et al. teaches compounds wherein the element "X" can be an amino acid sequence comprising between 10 to 30 amino acids. See Washburn et al. at paragraphs [0225], [0276], [0293], [0309], [0340], [0357], and [0426]. Nowhere does Washburn et a. teach or suggest that X can be amino acid sequence of 0-3 amino acids, as presently recited by Claim 1. Therefore, since Washburn et al. does not teach each and every element of Claim 1, Applicants respectfully submit that maintaining a rejection under 35 U.S.C. § 102(e) based on Washburn et al. is improper. Withdrawal of the rejection of Claim 1 under 35 U.S.C. § 102(e) as being anticipated by Washburn et al., is therefore respectfully requested. Allowance of Claim 1 is also respectfully requested.

With regard to the rejection of Claims 3-9, Applicants contend that Washburn et al. does not teach or suggest all the elements of these claims either. Since Claims 3-9 depend either directly or indirectly from Claim 1, and Washburn et al. does not teach or suggest all the elements of Claim 1 for the reasons stated above, Washburn et al. therefore does not teach or suggest all the elements of these dependent claims either. Accordingly, Applicants respectfully request withdrawal of the rejection of

Claims 3-9 on the basis of Washburn et al. Allowance of these claims is also respectfully requested.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

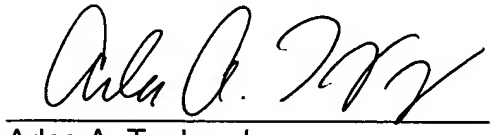
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON & TAYLOR, P.A.

Date: 04 Nov. 2004 By: 

Arles A. Taylor, Jr.
Registration No. 39,395

1392/10/3/2/2 AAT/JD/cht

Customer No: 25297